

## SEQUENCE LISTING

<110> BERDEL, Wolfgang E.  
MESTERS, Rolf M.

<120> Fusion polypeptides for antivascular tumor therapy

<130> 20490.003

<150> PCT/EP04/009364  
<151> 2004-08-20

<150> DE 10338733.1  
<151> 2003-08-22

<160> 41

<170> PatentIn version 3.1

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<213> Homo sapiens

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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys  
35 40 45

Cys Phe Tyr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val  
50 55 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala  
65 70 75 80

Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn  
85 90 95

Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr  
100 105 110

Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu  
115 120 125

Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg  
 130 135 140  
 Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser  
 145 150 155 160  
 Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu  
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 Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val  
 180 185 190  
 Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu  
 195 200 205  
 Cys Met Gly Gln Glu Lys Gly Glu Phe Arg Glu Ile Phe Tyr Ile Ile  
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 Gly Ala Val Val Phe Val Val Ile Ile Leu Val Ile Ile Leu Ala Ile  
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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys  
 35 40 45

Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val  
 50 55 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala  
 65 70 75 80

Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn  
 85 90 95

Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr  
 100 105 110  
 Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu  
 115 120 125  
 Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg  
 130 135 140  
 Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser  
 145 150 155 160  
 Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu  
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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys  
 35 40 45

Cys Phe Tyr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val  
 50 55 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala  
 65 70 75 80

Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn  
 85 90 95

Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr  
 100 105 110

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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys
35 40 45

Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val
50 55 60

Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala
65 70 75 80

Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn
85 90 95

Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr
100 105 110

Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu
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						180		185				190			
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Cys	Phe	Tyr	Thr	Thr	Asp	Thr	Glu	Cys	Asp	Leu	Thr	Asp	Glu	Ile	Val
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Gly	Asn	Val	Glu	Ser	Thr	Gly	Ser	Ala	Gly	Glu	Pro	Leu	Tyr	Glu	Asn
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Ser	Pro	Glu	Phe	Thr	Pro	Tyr	Leu	Glu	Thr	Asn	Leu	Gly	Gln	Pro	Thr
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							195		200			205			
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Val	Tyr	Thr	Val	Gln	Ile	Ser	Thr	Lys	Ser	Gly	Asp	Trp	Lys	Ser	Lys
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Cys	Phe	Tyr	Thr	Thr	Asp	Thr	Glu	Cys	Asp	Leu	Thr	Asp	Glu	Ile	Val
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Lys	Asp	Val	Lys	Gln	Thr	Tyr	Leu	Ala	Arg	Val	Phe	Ser	Tyr	Pro	Ala
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Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu		
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Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser		
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Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu		
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Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val		
180	185	190
Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu		
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Gly		
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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys		
35	40	45
Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val		
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Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala		
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Gly Asn Val Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn		

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Ser Pro Glu Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr			
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Ile Gln Ser Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu			
115	120	125	
Asp Glu Arg Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg			
130	135	140	
Asp Val Phe Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser			
145	150	155	160
Ser Ser Ser Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu			
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Ile Asp Val Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val			
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Ile Pro Ser Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu			
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Val Tyr Thr Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys  
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Cys Phe Tyr Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val  
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Lys Asp Val Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala

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Ser	Pro	Glu	Phe	Thr	Pro	Tyr	Leu	Glu	Thr	Asn	Leu	Gly	Gln	Pro	Thr
			100			105								110	
Ile	Gln	Ser	Phe	Glu	Gln	Val	Gly	Thr	Lys	Val	Asn	Val	Thr	Val	Glu
			115			120							125		
Asp	Glu	Arg	Thr	Leu	Val	Arg	Arg	Asn	Asn	Thr	Phe	Leu	Ser	Leu	Arg
			130			135							140		
Asp	Val	Phe	Gly	Lys	Asp	Leu	Ile	Tyr	Thr	Leu	Tyr	Tyr	Trp	Lys	Ser
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Ser	Ser	Ser	Gly	Lys	Lys	Thr	Ala	Lys	Thr	Asn	Thr	Asn	Glu	Phe	Leu
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Cys	Met	Gly	Gln	Glu	Lys	Gly	Glu	Phe	Arg	Gly	Cys	Val	Leu	Asn	Gly
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gacgagattg	tgaaggatgt	gaagcagacg	tacttggcac	gggtcttctc	ctacccggca											240
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	acacaccttacc	tggagacaaa	cctcggacag	ccaacaattc	agagtttga	acaggtggga	360
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 acaaaaagtga atgtgaccgt agaagatgaa cggactttag tcagaaggaa caacacttcc 420  
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gacgagattg tgaaggatgt gaagcagacg tacttggcac gggcttctc ctacccggca 240  
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tcaagttcag gaaagaaaaac agccaaaaca aacactaatg agttttgat tcatgtggat 540  
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gacgagattg tgaaggatgt gaagcagacg tacttggcac gggcttctc ctacccggca	240
gggaatgtgg agagcaccgg ttctgctgg gggctctgt atgagaactc cccagagttc	300
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<400> 15	
tcaggcacta caaatactgt ggcagcatat aatttaactt ggaaatcaac taatttcaag	60
acaattttgg agtgggaacc caaaccgtc aatcaagtct acactgttca aataagcact	120
aagtcaaggag attggaaaag caaatgcttt tacacaacag acacagagtg tgacctcacc	180
gacgagattg tgaaggatgt gaagcagacg tacttggcac gggcttctc ctacccggca	240
gggaatgtgg agagcaccgg ttctgctgg gggctctgt atgagaactc cccagagttc	300
acaccttacc tggagacaaa cctcggacag ccaacaattc agagtttga acaggtggaa	360
acaaaagtga atgtgaccgt agaagatgaa cggactttag tcagaaggaa caacacttcc	420
ctaagcctcc gggatgtttt tggcaaggac ttaatttata cacttttata ttggaaatct	480
tcaagttcag gaaagaaaac agccaaaaca aacactaatg agttttgat tgatgtggat	540
aaaggagaaa actactgttt cagtgttcaa gcagtgattc cctcccgAAC agttaaccgg	600
aagagtacag acagcccggt agagtgtatg ggccaggaga aaggggaaatt cagaggatgc	660

gtcttaatg gtaggatgga atgc

684

<210> 16  
<211> 45  
<212> DNA  
<213> Artificial

<220>  
<221> 5' Oligonucleotide primer for the preparation of tTF1-218  
<223> Synthetic construct

<400> 16  
catgccatgg gatcaggcac tacaatact gtggcagcat ataat

45

<210> 17  
<211> 40  
<212> DNA  
<213> Artificial

<220>  
<221> 3' Oligonucleotide primer for the preparation of tTF1-218  
<223> Synthetic construct

<400> 17  
cgggatccta ttatctgaat tcccctttct cctggccat

40

<210> 18  
<211> 45  
<212> DNA  
<213> Artificial

<220>  
<221> 5' Oligonucleotide primer for the preparation of tTF-GRGDSP  
<223> Synthetic construct

<400> 18  
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45

<210> 19  
<211> 43  
<212> DNA  
<213> Artificial

<220>  
<221> 3' Oligonucleotide primer for the preparation of tTF-GRGDSP  
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43

<210> 20  
<211> 45  
<212> DNA  
<213> Artificial

<220>  
<221> 5' Oligonucleotide primer for the preparation of tTF-GNGRAHA  
<223> Synthetic construct

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<210> 21  
<211> 46  
<212> DNA  
<213> Artificial

<220>  
<221> 3' Oligonucleotide primer for the preparation of tTF-GNGRAHA  
<223> Synthetic construct

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<210> 22  
<211> 45  
<212> DNA  
<213> Artificial

<220>  
<221> 5' Oligonucleotide primer for the preparation of tTF-GCNGRCG  
<223> Synthetic construct

<400> 22  
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<210> 23  
<211> 46  
<212> DNA  
<213> Artificial

<220>  
<221> 3' Oligonucleotide primer for the preparation of tTF-GCNGRCG  
<223> Synthetic construct

<400> 23  
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<210> 24  
<211> 45  
<212> DNA  
<213> Artificial

<220>  
<221> 5' Oligonucleotide primer for the preparation of tTF-GCNGRCVSGCAGRC  
<223> Synthetic construct

<400> 24  
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<210> 25  
<211> 67  
<212> DNA  
<213> Artificial

<220>  
<221> 3' Oligonucleotide primer for the preparation of tTF-GCNGRCVSGCAGRC  
<223> Synthetic construct

<400> 25  
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attcccc 67

<210> 26  
<211> 45  
<212> DNA  
<213> Artificial

<220>  
<221> 5' Oligonucleotide primer for the preparation of tTF-GCVLNGRMEC  
<223> Synthetic construct

<400> 26  
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<210> 27  
<211> 55  
<212> DNA  
<213> Artificial

<220>  
<221> 3' Oligonucleotide primer for the preparation of tTF-GCVLNGRMEC  
<223> Synthetic construct

<400> 27  
cgggatccta ttagcattcc atcctaccat ttaagacgca tcctctgaat tcccc 55

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<210> 28
<211> 45
<212> DNA
<213> Artificial

<220>
<221> 5' Oligonucleotide primer for the preparation of tTF-GALNGRSHAG
<223> Synthetic construct

<400> 28
catgccatgg gatcaggcac tacaaatact gtggcagcat ataat 45

<210> 29
<211> 55
<212> DNA
<213> Artificial

<220>
<221> 3' Oligonucleotide primer for the preparation of tTF-GALNGRSHAG
<223> Synthetic construct

<400> 29
cgggatccta ttaaccagcg tgagatcttc catttaaagc acctctgaat tcccc 55

<210> 30
<211> 45

<212> PRT

<213> Artificial

<220>
<221> Amino acid sequence of the affinity-tag
<223> Synthetic construct

<400> 30
His His His His His Ser Ser Gly Leu Val Pro Arg Gly Ser Gly
1 5 10 15

Met Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser
20 25 30

Pro Asp Leu Gly Thr Asp Asp Asp Lys Ala Met Gly
35 40 45

<210> 31
<211> 269
<212> PRT

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<213> Artificial

<220>

<221> Amino acid sequence of tTF-GRGDSP having an N-terminal affinity-tag  
<223> Synthetic construct

<400> 31

His His His His His Ser Ser Gly Leu Val Pro Arg Gly Ser Gly  
1 5 10 15

Met Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser  
20 25 30

Pro Asp Leu Gly Thr Asp Asp Asp Lys Ala Met Gly Ser Gly Thr  
35 40 45

Thr Asn Thr Val Ala Ala Tyr Asn Leu Thr Trp Lys Ser Thr Asn Phe  
50 55 60

Lys Thr Ile Leu Glu Trp Glu Pro Lys Pro Val Asn Gln Val Tyr Thr  
65 70 75 80

Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys Cys Phe Tyr  
85 90 95

Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val Lys Asp Val  
100 105 110

Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala Gly Asn Val  
115 120 125

Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn Ser Pro Glu  
130 135 140

Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr Ile Gln Ser  
145 150 155 160

Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu Asp Glu Arg  
165 170 175

Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg Asp Val Phe  
180 185 190

Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser Ser Ser Ser  
195 200 205

Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu Ile Asp Val  
210 215 220

Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val Ile Pro Ser  
225 230 235 240

Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu Cys Met Gly  
245 250 255

Gln Glu Lys Gly Glu Phe Arg Gly Arg Gly Asp Ser Asp

260

265

<210> 32  
<211> 270  
<212> PRT  
<213> Artificial

<220>  
<221> Amino acid sequence of tTF-GNGRAHA having an N-terminal affinity-tag  
<223> Synthetic construct

<400> 32  
His His His His His Ser Ser Gly Leu Val Pro Arg Gly Ser Gly  
1 5 10 15

Met Lys Glu Thr Ala Ala Ala Lys Phe Glu Arg Gln His Met Asp Ser  
20 25 30

Pro Asp Leu Gly Thr Asp Asp Asp Lys Ala Met Gly Ser Gly Thr  
35 40 45

Thr Asn Thr Val Ala Ala Tyr Asn Leu Thr Trp Lys Ser Thr Asn Phe  
50 55 60

Lys Thr Ile Leu Glu Trp Glu Pro Lys Pro Val Asn Gln Val Tyr Thr  
65 70 75 80

Val Gln Ile Ser Thr Lys Ser Gly Asp Trp Lys Ser Lys Cys Phe Tyr  
85 90 95

Thr Thr Asp Thr Glu Cys Asp Leu Thr Asp Glu Ile Val Lys Asp Val  
100 105 110

Lys Gln Thr Tyr Leu Ala Arg Val Phe Ser Tyr Pro Ala Gly Asn Val  
115 120 125

Glu Ser Thr Gly Ser Ala Gly Glu Pro Leu Tyr Glu Asn Ser Pro Glu  
130 135 140

Phe Thr Pro Tyr Leu Glu Thr Asn Leu Gly Gln Pro Thr Ile Gln Ser  
145 150 155 160

Phe Glu Gln Val Gly Thr Lys Val Asn Val Thr Val Glu Asp Glu Arg  
165 170 175

Thr Leu Val Arg Arg Asn Asn Thr Phe Leu Ser Leu Arg Asp Val Phe  
180 185 190

Gly Lys Asp Leu Ile Tyr Thr Leu Tyr Tyr Trp Lys Ser Ser Ser Ser  
195 200 205

Gly Lys Lys Thr Ala Lys Thr Asn Thr Asn Glu Phe Leu Ile Asp Val  
210 215 220

Asp Lys Gly Glu Asn Tyr Cys Phe Ser Val Gln Ala Val Ile Pro Ser

225 230 235 240

Arg Thr Val Asn Arg Lys Ser Thr Asp Ser Pro Val Glu Cys Met Gly  
245 250 255

Gln Glu Lys Gly Glu Phe Arg Gly Asn Gly Arg Ala His Ala  
260 265 270

<210> 33

<211> 6

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<400> 33

Gly Arg Gly Asp Ser Pro  
1 5

<210> 34

<211> 7

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<400> 34

Gly Asn Gly Arg Ala His Ala  
1 5

<210> 35

<211> 10

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<400> 35

Gly Ala Leu Asn Gly Arg Ser His Ala Gly  
1 5 10

<210> 36

<211> 7

<212> PRT

<213> Artificial

<220>

<221> Cyclic  
<223> Synthetic construct

<400> 36

Gly Cys Asn Gly Arg Cys Gly  
1 5

<210> 37  
<211> 14  
<212> PRT  
<213> Artificial

<220>  
<221> Cyclic  
<223> Synthetic construct

<400> 37

Gly Cys Asn Gly Arg Cys Val Ser Gly Cys Ala Gly Arg Cys  
1 5 10

<210> 38  
<211> 10  
<212> PRT  
<213> Artificial

<220>  
<221> Cyclic  
<223> Synthetic construct

<400> 38

Gly Cys Val Leu Asn Gly Arg Met Glu Cys  
1 5 10

<210> 39  
<211> 10  
<212> PRT  
<213> Artificial

<220>  
<223> Synthetic Construct

<400> 39

Thr Ala Ala Ser Gly Val Arg Ser Met His  
1 5 10

<210> 40  
<211> 10  
<212> PRT

<213> Artificial

<220>

<223> Synthetic Construct

<400> 40

Leu Thr Leu Arg Trp Val Gly Leu Met Ser  
1 5 10

<210> 41

<211> 8

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<400> 41

Thr Thr His Trp Gly Phe Thr Leu  
1 5